REMARKS

The Amendments

Applicants have amended claim 10 to recite that the compound is an inhibitor or ligand of said first serine/threonine or tyrosine protein kinase, to provide a description for "Ki" and "Kd", and to improve its form. Support for these amendments may be found throughout the specification. See, e.g., page 9, lines 12-18. Applicants have amended claim 11 to depend from added claim 23 and have amended claim 12 to improve its form. Support for these amendments may be found throughout the specification. See, e.g., page 1, lines 5-6 and 13-14. Applicants have added claim 23. Support may be found throughout the specification. See, e.g., page 1, lines 5-6 and 13-14 and page 17, lines 6-13.

The Election/Restriction

Applicants affirm their election of species ERK2, which was made without traverse in their September 26, 2002 response.

Sequence Rules Compliance

Applicants acknowledge with appreciation Examiner's statement that the Sequence Listing complies with the Requirement for Patent Applications Containing Nucleotide Sequence and/or Amino Acid Sequence Disclosures, and note that the Statement Under 37 C.F.R. § 1.821(e) was originally filed August 18, 2000.

Information Disclosure Statement

Applicants acknowledge with appreciation the Examiner's consideration of the Information Disclosure Statement filed June 11, 2002. Applicants request that the Examiner consider the Information Disclosure Statement and cited documents filed August

18, 2000 and return with the next communication a copy of the Form PTO-1449 as considered and initialed by the Examiner.

The Claim Objections

The Examiner has objected to claim 10 because he states that the terms "Ki" and "Kd" are abbreviations.

Applicants have amended claim 10 to recite that Ki is "a dissociation constant for said inhibitor" and Kd is "a dissociation constant for said ligand", thus obviating the objection.

The Rejection Under 35 U.S.C. § 112, Second Paragraph

The Examiner states that claims 10-13 are rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite. Specifically, the Examiner states that it is unclear in paragraph (b) of claim 10 what is meant by the phrase "said binding of the compound with the mutant having a Ki or a Kd", because Ki is known to refer to the binding constant of an enzyme to an inhibitor and no inhibitor is recited in the claim. Applicants traverse.

Applicants have amended claim 10 to recite that the compound may be a ligand or an inhibitor such that the recitation of both "Kd" and "Ki" is appropriate. Thus, applicants have obviated the rejection.

The Rejections Under 35 U.S.C. § 102

The Examiner states that claim 10 is rejected under 35 U.S.C. § 102(a) as allegedly being anticipated by Shah et al., *Proc. Natl. Acad. Sci. USA* 94: 3565-3570, April

1997 (hereafter "Shah"). The Examiner contends that Shah teaches mutants of protein tyrosine kinase v-Src that have mutations in their ATP binding sites. The Examiner also contends that Shah teaches that one of the mutants is GST-XD4, which binds to ATP with a Km of 12 $\pm$ 3 μM. The Examiner contends that since the Km for GST-XD4 binding to ATP may be 9 μM, the binding of the compound ATP to a mutant GST-XD4 had a Kd less than 10 μM, as recited in claim 10. Applicants traverse.

Contrary to the Examiner's assertion, GST-XD4 does not have mutations in its ATP binding site. Shah discloses that GST refers to glutathione *S*-transferase, and that XD4 refers to the Δ(77-225) fragment of v-Src, which contains the ATP-binding site of v-Src. See footnote on page 3565, right column, and Figure 4 on page 3568 of Shah. Shah also states that GST-XD4 is the wild-type kinase and that GST-XD4 (V323A, I338A) is the mutant form of the kinase. See, e.g., page 3569, left column. Thus, GST-XD4 does not have at least one amino acid substitution in its ATP binding site compared to the naturally occurring protein kinase, as required by claim 10. Further, although Shah demonstrates that the wild-type kinase binds to ATP with a Km of 12 $\pm$ 3 μM, the mutant kinase described by Shah binds to neither ATP nor N^6-(cyclopentyl) ATP with a Km of less than 10 μM. See Table 1 on page 3569 of Shah. Thus, Shah does not anticipate claim 10.

The Examiner states that claim 10 is rejected under 35 U.S.C. § 102(e) as allegedly being anticipated by United States Patent 6,390,821 to Shokat (hereafter "the '821 patent"). Similar to Shah, the Examiner contends that the '821 patent teaches a mutant of protein tyrosine kinase v-Src, GST-XD4, that has mutations in its ATP binding sites and that binds to ATP with a Km of 12$\pm$3 μM. The Examiner contends that the binding of the

compound ATP to a mutant GST-XD4 may have a Kd less than 10 μM, thus anticipating claim 10. Applicants traverse.

First, the '821 patent cannot be used as prior art under 35 U.S.C. § 102(e) with respect to the instant application because the § 102(e) date of the '821 patent is after the effective filing date of the instant application. The instant application is a continuation of PCT/US99/03181, filed February 16, 1999, which in turn claims benefit from United States application 09/025,580, filed February 18, 1998. Thus, the instant application has an effective filing date of February 18, 1998. In contrast, the '821 patent has a 35 U.S.C. § 102(e) date of November 17, 1999, which is more than a year after the effective filing date of the instant application. See, e.g., the front page of the '821 patent. Although the Examiner asserts that the priority date of the '821 patent is February 7, 1997, this date cannot be used for prior art purposes because an international application filed prior to November 29, 2000 "may not be used to reach back (bridge) to an earlier filing date through a priority or benefit claim for prior art purposes under 35 U.S.C. § 102(e)." See "Examination Guidelines for 35 U.S.C. § 102(e), as amended by the American Inventors Protection Act of 1999, and further amended by the Intellectual Property and High Technology Technical Amendments Act of 2002, and 35 U.S.C. § 102(g) (Revised)", (hereafter "the 102(e) Examination Guidelines"), page 3. Further, even if the international application from which the '821 patent issued via 35 U.S.C. § 371 properly claimed priority and/or benefit to any earlier-filed provisional or non-provisional U.S. applications, there is no 102(e) date for these U.S. applications or for the PCT application itself. See the 102(e) Examination Guidelines, page 14. Thus, the '821 patent does not anticipate claim 10 because its 102(e) date is after the effective filing date of the instant application.

Second, as discussed above for Shah, GST-XD4 does not have mutations in its ATP binding site. Rather, the '821 patent discloses that GST-XD4 is the wild-type form of v-Src. See, e.g., column 29, lines 9-19, column 30, lines 21-31 and Figure 1 of the '821 patent. Thus, GST-XD4 does not have at least one amino acid substitution in its ATP binding site compared to the naturally occurring protein kinase, as required by claim 10. Similar to Shah, the '821 patent states only that the wild-type kinase binds to ATP with a Km of 12 ± 3 μM. See Table 1, column 31, of the '821 patent.

Conclusion

In view of the foregoing amendments and remarks, applicant requests that the Examiner withdraw the claim rejections and allow all claims of this application. If the Examiner believes that an interview would facilitate the resolution of any outstanding issues, he is kindly requested to contact the undersigned.

Respectfully submitted,

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APPENDIX OF AMENDMENTS

10. (Twice amended) A mutant of a naturally occurring second serine/threonine protein kinase or tyrosine protein kinase, said mutant characterized by:

[a.] (a) having an ATP binding site comprising at least one amino acid substitution compared to an ATP binding site of the naturally occurring second serine/threonine protein kinase or tyrosine protein kinase; and

[b.] (b) having the ability to bind to a compound that binds to an ATP binding site of a first serine/threonine protein kinase or first tyrosine protein kinase, wherein said compound is an inhibitor or a ligand of said first serine/threonine protein kinase or said first tyrosine kinase, said binding of the compound with the mutant having a dissociation constant for said inhibitor (Ki) or a dissociation constant for said ligand (Kd) that is

(i) less than 10 μM and

[c.] (ii) at least 10-fold lower than the Ki or Kd of the binding of said compound with said naturally-occurring second serine/threonine protein kinase or second tyrosine protein kinase.

11. (Twice amended) The mutant second protein kinase according to claim [10] 23, wherein said first and said second protein kinases are mitogen activating protein (MAP) kinases.

12. (Twice amended) The mutant second protein kinase according to claim 11, wherein said mutant second protein kinase is selected from:

[a.] (a) a mutant extracellular-signal regulated kinase 2 (ERK2) comprising the amino acid sequence of SEQ ID NO:2, wherein amino acid 105 is threonine or alanine; or

[b.] (b) a mutant Jun-N-terminal kinase 3 (JNK3) comprising amino acids 40-402 of SEQ ID NO:3, wherein amino acid 146 is threonine or alanine.